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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,613	10/26/2001	Jason C. H. Shih	4171-102 CIP	4213

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
PO BOX 14329
RESEARCH TRIANGLE PARK, NC 27709

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,613	H. SHIH, JASON C.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *1-38, 66-70 and 75-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-65, 71-74, and 80-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2, 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, and the species wherein the proteolytic enzyme is a keratinase in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-38, 66-70, and 75-79 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, or species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Claims 39-65, 71-74, and 80-83 are under consideration to the extent that they read on the elected inventions.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on January 31, 2002 and May 19, 2003, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

4. It is noted that the following references are listed in the above IDS' are in a foreign language accompanied by an English abstract. Due to this, the references have been examined only to the extent of the disclosure in the abstract.

WO 00/58344 (reference AK of the January 2002 IDS)
WO 01/09287 (reference AP of the January 2002 IDS)

5. Each of the following reference listing in the above IDS' were submitted only as foreign language documents, with no English translation, abstract, or explanation of their relevance. These documents have therefore not been considered.

EP 0 667 352 (reference BD of the January 2002 IDS)
EP 0 530 173 (reference BE of the January 2002 IDS)
JP 11049611 (reference BF of the January 2002 IDS)
JP 11032795 (reference BG of the January 2002 IDS)

Claim Objections

6. Claims 51-61, and 72 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The identified claims each recite method steps presumable intended to be carried out in the use of the claimed composition. However, none of these steps further identifies of limits the claimed composition.

For the purposes of this action, and because the independent claims are drawn to compositions of matter, the identified claims are interpreted as product claims indicating the intended use of the claimed product. See, MPEP § 2114.01.

7. Claims 64 and 65 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Each of these claims depends from claim 39, which

reads on a system comprising a proteolytic enzyme. From this language, it appears that the claim reads on the complete molecules of enzymes capable of degrading proteinaceous materials. Thus, claims 64 and 65, which expand the scope of the claims to read on fragments of such enzymes, are not properly dependant on claim 39.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 39-41, 44-53, and 56-62, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed products that are capable of reducing the presence of prion protein on an article by heating it with a heating means to a temperature range of 100° to about 150° C and then exposing it to a proteolytic enzyme, does not reasonably provide enablement for the claimed system wherein the system is capable of disinfecting the instruments at temperatures of less than 100°C and exposure to any proteolytic enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims read on systems for the disinfection of articles susceptible to prion contamination comprising the article, means for heating the articles to a sufficient temperature to enhance proteolytic susceptibility, a proteolytic enzyme effective for at least partial reduction of the prion proteins, and means for exposing the articles to the enzymes. It is noted that, although

the claims read on a composition of matter, several of the dependant claims describe functional limitations of the claimed invention. Because the claims are directed to a composition of matter, these function claims are read as defining an intended use of the claimed composition. See, MPEP § 2112.01. Thus, the claims are rejected because the Applicant has specified an intended use that is not supported by the teachings of the art or the specification.

As indicated above, the claims broadly read on the claimed composition such that the composition is capable of disinfecting an article from prion proteins when used in a method wherein the article is heated to any temperature between about 35° and 150° C and subsequently subjected to any proteolytic enzyme. It is noted that, in the present application, the Applicant has provided no working examples of the claimed invention. However, in the application to which priority is presently claimed as a CIP (now U.S. Patent 6,613,505), the Applicant does demonstrate that a keratinase was effective at degrading prions without cooking. See, columns 10-11 of the patent. However, Bolton et al., teaches that, although treatment of prions with proteinase K and without prior denaturation (heating) of the protein did lead to some decreases in prion concentration, treatment with other proteases in like circumstances did not result in a change in prion concentration. See, Bolton et al., Biochemistry, 23: 598-5906. Thus, the art teaches that while some proteases would be capable of reducing prion proteins heated to a temperature of less than 100° C in the presence of SDS, such would not be the case with any protease.

There are large number of proteases known in the art, as can be demonstrated by the Applicant's listing of several generic types of proteases. See e.g., claim 73. Thus, it is apparent from the art that treatment of prions with less than 100° C would not render the protein

susceptible to all of these proteases. As the Applicant has not provided any guidance as to what temperatures may provide sufficient denaturation for the use of any particular protease, the Applicant has therefore not provided adequate information for those in the art to practice the claimed invention to its full extent without undue experimentation. This is because in order for those skilled in the art to use the claimed invention to the full scope as claimed, they would have to discover for themselves which proteases are and are not capable of degrading prions that have not been heated to at least 100° C.

10. Claims 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for systems comprising a complete keratinase or B. licheniformis PWD-1 enzyme, does not reasonably provide enablement for systems comprising only enzymatically active fragments of these enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Although the claims are broadly drafted to read on systems comprising both whole, and active fragments of, proteolytic enzymes, the Applicant has not provided any teachings with reference to the identified enzymes such that those in the art would know what fragments of any of these enzymes would be capable of cleaving a protein.

As indicated above, the Applicant has provided no teachings regarding what fragments of a keratinase enzyme would be effective in cleaving proteins. Those in the art have accepted that one cannot generally distinguish what parts of the protein are necessary for protein function. See e.g. Bork, Genome Res 10: 398-400 (teaching that those in the art are generally not capable of

achieving greater than 70% accuracy in determining the functions of a protein sequence); and Bowie et al., Science 247: 1306-10 (teaching that the effects of a substitution or other alteration to a particular amino acid on a protein's activity are generally unpredictable). Each of the Bork and Bowie references therefore indicates that the art of protein modification is complex and unpredictable. Thus, absent teachings in the art or by the Applicant as to what residues are required for keratinases in general, or for any keratinase in specific, to cleave proteins, those in the art would not have sufficient information to practice the claimed invention to its full extent. Rather, in order to do so, those in the art would first have to determine for themselves what fragments of what enzymes would be capable of performing the required functions. The Applicant is therefore not enabled for the claimed systems to the extent that they read on systems including other than whole proteolytic keratinases.

11. Claims 81 and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection. There does not appear to be any descriptive support in the application for a "means for verifying the disinfection of articles with respect to prion contamination." While the Applicant does indicate that, with regards to methods for the removal of prions from a tissue, a test for the verification of infectious prions within the tissue may be included, there is no support in the application as filed for a means for verifying the removal of prions from an instrument treated for disinfection of prions.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 39-64, and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of the World Health Organization (WHO) document identified as reference BT in the March 2003 IDS in view of Huth et al. (U.S. Patent 6,448,062), Vlass et al. (U.S. Patent 6,210,639), and Potgeiter et al. (U.S. H1,818), and further in view of the teachings of Bolton (supra) and Oesch et al. (Biochemistry 33: 5926-31). The rejected claims read on systems for the disinfection of articles comprising the articles to be disinfected, means for heating the articles, proteolytic enzymes, and mans for exposing the articles to the enzymes. Among the enzymes included in the system are keratinase enzymes.

The WHO document teaches methods for the sterilization of medical devices from prion infection by treating the device with heat, and then treating the devices with routine sterilization. Page 14, and page 29 (Annex III). Thus, the reference teaches the disinfection of such devices with a system comprising the articles, a heating device, and a sterilizing solution used routinely in the art. The reference does not, however, teach that the sterilization solution comprises a proteolytic enzyme.

Each of Huth, Vlass, and Potgeiter teach compositions useful for the disinfection or cleaning of medical instruments. Huth teaches that numerous types of enzymes may be used in a medical sterilization solution. See e.g., cols 14-15. Similar teachings are provided by Vlass (col 1, lines 49 an d50, col. 2, lines 22-28, and col 5) and by Potgeiter (col 10, lines 43-51, and cols 14-15). Each of these references also identifies keratinases as enzymes useful in these compositions. In addition, Potgeiter also teaches that other components are often included in the sterilization solutions with proteolytic enzymes, including builders and surfactants. The Vlass reference further indicates that the concentration of the enzyme is preferable between .1 to 10 mg per 10 ml (equivalent to .01 to 1 g per L). Thus, it would have been obvious to those in the art to use the enzymes at an appropriate concentration within this range. See e.g., Huth, columns 17-18 (indicating that the concentration of enzymes used in a cleaning solution varies depending on several factors). The Applicant's concentration range is therefore obvious as optimization of a known composition. Thus, in view of the teachings of the WHO document, and the Huth, Vlass, and Potgeiter references, it would have been obvious to those in the art to have a system for cleaning of medical articles of prion proteins comprising the articles, a means of heating the articles, a proteolytic enzyme, and means for exposing the instruments to the enzyme.

The art therefore indicates that the identified system may be used with regards to medical instrument. It is known in the art that such instruments of necessity must be rendered safe from passing infection. In view of this, it would have been equally obvious to those in the art to use such a system for other types of instruments susceptible to infection by prion proteins.

It is noted that, because the combination suggested by the WHO document appears to contain all of the structural elements of the claimed system, it is presumed that the combination

would also have the same functionality as the claimed system. Further, those skilled in the art would have further grounds to have had a reasonable expectation of success that the system would be useful for the purposes indicated by the Applicant due to the additional teachings of Bolton and Oesch.

As indicated above, Bolton teaches that purified prion may be deactivated by exposure to an enzyme after being heated to 100° C in a solution. Abstract. Further, the reference indicates that the susceptibility to degradation by the enzyme was due to the denaturation of the protein. See, pages 5900-01. See also Oesch, page 5928 (also indicating that prions become susceptible to protease degradation after being denatured). Thus, Bolton indicates that heating of enzymes to high temperature (as taught by the WHO document) would result in the denaturation of the prion proteins. Thus, because each of Bolton and Oesch further indicate that denatured prions are susceptible to degradation by proteolytic enzymes, those in the art would have expected the combination suggested by the WHO document, Huth, Vlass, and Potgeiter to be effective in the degradation of prion. This is because they would have expected the heating device suggested by the WHO document to both inactivate and denature the proteins, and that the cleaning agents comprising the enzymes suggested by the other three references would then be effective in further inactivating and degrading the proteins. The references therefore render the claimed system obvious.

While the Applicant has attempted to further identify the system by inclusion of claims with functional language, these claims are not effective in distinguishing the claimed composition from those suggested by the art. This is because, as indicated above, these claims merely recite intended uses of the claimed system. As the composition of the art shares all of the

claimed structural characteristics with the claimed system, and would therefore be capable of performing these functions, such claims are not effective to distinguish over the prior art.

14. Claims 65, 74, 80, and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over the WHO reference, Vlass, Huth, Potgeiter, Bolton, and Oesch as applied to claims 39-64, and 71-73 above, and further in view of Shih et al. (U.S. Patent 5,171,682). These claims read on the system described above, wherein the keratinase enzyme is the B. licheniformis PWD-1 keratinase. As indicated above, each of the references of Vlass, Huth, and Potgeiter indicate that keratinase enzymes would be useful in the systems suggested by the WHO document. The Shih reference identified the PWD-1 enzyme as a keratinase. It would therefore have been obvious to those in the art to have used the enzyme disclosed by Shih in the solutions described by Vlass, Huth, and Potgeiter as these references indicate that any keratinase may be used.

15. Claims 81 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over the WHO reference, Vlass, Huth, Potgeiter, Bolton, Oesch and Shih as applied against claims 39-65, 71-74, 80, and 82 above, further in view of any of Darbord (supra), Taylor et al., (J Gen Virol 77: 3161-64), or Belhumeur et al. (WO 00/65344). Claims 81 and 84 describe the claimed system, but further require the presence of a means for the verifying the disinfection of the articles of prion contamination. The art teaches both the use of the claimed system to reduce the presence of prion infectivity from articles, and that prion proteins are highly resistant to decontamination and are infectious. See e.g., WHO document (pages 1, 2-3, and 14-15); and Darbord (Biomed & Pharmacother 53:34-38, page 34- of record in the Jan 2002 IDS). It would

therefore have been obvious to those in the art to verify the decontamination of tools had been cleared of the infectious particles.

It is further noted that the art indicates that a limited means have been developed for detection of prion particles on disinfected articles. See e.g., Darbord, page 35, and Taylor (page 3161). Another method of measuring the efficacy of an anti-prion sterilization process was suggested by Belhumeur. See, abstract. Thus, it would have been obvious to those in the art to use such methods to verify the efficacy of disinfection against prions due to prions' decontamination resistant, infectious, and deadly nature.

Conclusion

16. No claims are allowed.

17. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Le et al., Ann Rech Vet 21.: 75-79. This reference is relevant in that it demonstrates that it was known in the art that prions (as the infective agent of scrapie) were subject to degradation by certain proteolytic enzymes (or combinations thereof- e.g., the Proase enzyme conglomeration).
>
> Ingemanson, WO 00/38742 (of record in the January 2002 IDS). This reference indicates that elevated temperatures alone are not sufficient to sterilize devices of infectious prion proteins. Page 3, lines 4-20.
>
> Reichel et al., U.S. Patent 5,633,349 (of record in the January 2002 IDS). This reference teaches a method of sterilizing a biological sample of prions comprising the heating and addition of a chaotropic (denaturing) agent selected from wither urea or thiocyanate to the sample. See also, U.S. Patent 5,317,092, claim 4 (indicating that each of these chaotropic agents are protein denaturing agents).

McKinley et al., Cell 35: 57-62 (of record in the January 2002 IDS). This reference teaches that PrP^{SC} is resistant to digestion by proteolytic enzymes, but that such digestion does occur after denaturation of the protein. Pages 60-61.

Kocisko et al, Biochemistry, 35 : 13434-42. This reference teaches that denaturation of prions increases their susceptibility to proteases.

Darbord et al., Biomed and Pharmacother 53: 34-38 (of record in the Jan 2002 IDS). This reference teaches that one method used for sterilization of re-usable instruments is through autoclaving (heating) the instruments to a temperature of 134-138° C. Page 37.

Rutala et al., Helathcare Epidemiology CID 32: 1348-56 (reference BM in the Jan 2002 IDS). This reference provides similar teachings to those of Darbord. See, Rutala, pages 1353-1354). The reference also indicates that cleaning with enzymatic detergents should also be undertaken. Page 1354. The reference further suggests that studies be undertaken of the disinfection of prions by sterilization or disinfection (e.g. with heat) after cleaning with the enzymatic compositions. However, as the reference is merely suggesting the study, the reference qualifies only as showing that the claimed invention was obvious to try.

Meyer et al., J Virol 73 : 9386-92. This reference teaches the preparation of prion samples using proteinase K and a heating device. See, page 9388 (section titled Ultracentrifugation and proteinase K digestion). However, the method disclosed (and therefore the system used) does not involve the decontamination of instruments. Nor does the disclosed system appear to include a means for exposing a heated instrument to a proteolytic enzyme. The reference is therefore relevant in that it teaches a system comprising two of the elements of the claimed system, lacking either the articles or the means for exposure required by the claims.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner

JAMES HOUSEL 12/15/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600